Notice of Allowability	Application No.	Applicant(s)	
	10/775,640	BAKKER ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *30 April 2007 and 06 June 2007*.

2. ☒ The allowed claim(s) is/are *21-38, renumbered as claims 1-18, respectively*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Eileen B O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Sheela Mohan-Peterson on August 14, 2007.

The application has been amended as follows:

Claim 27, second line, "1-87 of SEQ ID NO: 2 or 6" has been replaced with – 1-87 of SEQ ID NO: 2 or 1-88 of SEQ ID NO: 6 – .

Claim 28, second line, "2-87 of SEQ ID NO: 2 or 6" has been replaced with – 2-87 of SEQ ID NO: 2 or 2-88 of SEQ ID NO: 6 – .

In claim 35, "a toxin or" has been deleted.

In claim 37, on the second line, "nd" has been replaced with – and – .

The following amendments were filed 30 April, 2007 by Applicants, but not entered due to a technical problem, and are incorporated herein.

Please amend the specification as follows:

Please replace the paragraph beginning at page 1, line 4, with the following rewritten paragraph:

-- This filing is a divisional of ~~co-pending application~~ USSN 10/191,732, filed July 8, 2002, now US Patent No. 6,953,843, which ~~claims benefit from a Divisional~~ is a divisional of USSN 09/127,946, filed July 31, 1998, now U.S. Patent No. 6,416,973, ~~issued July 9, 2002,~~

which claims benefit of U.S. Provisional Patent Applications 60/089,168, filed June 12, 1998; 60/069,639, filed December 15, 1997; 60/063,717, filed October 29, 1997; 60/069,692, filed December 16, 1997; and 60/054,430, filed August 1, 1997; each of which is incorporated herein by reference.-

Please replace the paragraph beginning on page 3, line 17, with the following rewritten paragraph:

--Binding compounds are also provided, comprising an antigen binding portion from an antibody, which specifically binds to: a natural DAP12 polypeptide, wherein the antibody: is raised against a mature polypeptide of ~~Table 1~~ SEQ ID NO:2 or 6; is immunoselected; is a polyclonal antibody; binds to a denatured DAP12; exhibits a Kd to antigen of at least 30 μM; is attached to a solid substrate, including a bead or plastic membrane; is in a sterile composition; or is detectably labeled, including a radioactive or fluorescent label; or a natural DAP10 polypeptide, wherein the antibody: is raised against a mature polypeptide ~~of Table 2~~ SEQ ID NO: 8 or 10; is immunoselected; is a polyclonal antibody; binds to a denatured DAP10; exhibits a Kd to antigen of at least 30 μM; is attached to a solid substrate, including a bead or plastic membrane; is in a sterile composition; or is detectably labeled, including a radioactive or fluorescent label; or a natural MDL-1 polypeptide, wherein the antibody: is raised against a mature polypeptide of :Faigle-8 SEQ ID NO: 12 or 14; is immunoselected; is a polyclonal antibody; binds to a denatured MDL-1; exhibits a Kd to antigen of at least 30 μM; is attached to a solid substrate, including a bead or plastic membrane; is in a sterile composition; or is detectably labeled, including a radioactive or fluorescent label. Various kits are provided, e.g., comprising the binding compound, and: a compartment comprising the binding compound; and/or instructions for use or disposal of reagents in the kit. Additional embodiments include a composition comprising: a sterile binding compound, or the binding compound and a carrier, wherein the carrier is: an aqueous compound, including water, saline, and/or buffer; and/or formulated for oral, rectal, nasal, topical, or parenteral administration. --

Please replace the paragraph beginning on page 4, line 1, with the following rewritten paragraph:

-- Nucleic acid embodiments include an isolated or recombinant nucleic acid encoding these polypeptides, wherein the nucleic acid encodes an antigenic peptide sequence ~~of Table 1,2, or 3~~ SEQ ID NO: 2, 6, 8, 10, 12, or 14. Preferred embodiments include such a nucleic acid, which encodes a plurality of antigenic peptide sequences of the table. Other nucleic acids include one which: is an expression vector; further comprises an origin of replication; is from a natural source; comprises a detectable label; comprises synthetic nucleotide sequence; is less than 6 kb, preferably less than 3 kb; is from a mammal, including a primate or rodent; comprises a natural full length coding sequence; is a hybridization probe for a gene encoding DAP12, DAP10, or MDL- 1; or is a PCR primer, PCR product, or mutagenesis primer--

Please replace the paragraph beginning on page 7, line 17, with the following rewritten paragraph:

-- Table 1 discloses both the nucleotide sequence (SEQ ID NO: 1 and 5) of the cDNA and the corresponding amino acid sequence for DAP12 embodiments. The primate nucleotide sequence corresponds to SEQ ID NO: 1; the amino acid sequence corresponds to SEQ ID NO: 2. The signal sequence appears to run from met(-26) to gln(-1) or alal ; the mature protein should run from about alal (or gln2), the extracellular domain from about alal to pro14; the extracellular domain contains two cysteines at 7 and 9, which likely allow disulfide linkages to additional homotypic or heterotypic accessory proteins; the transmembrane region runs from about gly15 or val6 to about gly39; and an ITAM motif from tyr65 to leu79 (YxxL-6/8x-YxxL). The LVA03A EST was identified and used to extract other overlapping sequences. See also Genbank Human ESTs that are part of human DAP12; some, but not all, inclusive Genbank Accession # AA481924; H39980; W60940; N41026; R49793; W60864; W92376; H12338; T52100; AA480109; H12392; W74783; and T55959.--

Please replace the paragraph beginning on page 10, line 1, with the following rewritten paragraph:

-- Table 2 discloses both the nucleotide sequence of the cDNA and the corresponding amino acid sequence (SEQ ID NO: 7, 8, 9, and 10) of each of the human and mouse DAP10 genes. The nucleotide sequence for human corresponds to SEQ ID NO: 7; the amino acid sequence corresponds to SEQ ID NO: 8. The signal sequence appears to run from about met(-18) to ala(-1); the mature protein should run from about gln1, the extracellular domain from about gln1 to pro30; the extracellular domain contains two cysteines at 21 and 24, which likely allow disulfide linkages to additional homotypic or heterotypic accessory proteins; the transmembrane region runs from about leu31 to val47, with a characteristic charged residue corresponding to asp39; and an interesting YxxM motif from tyr67 to met70, which is similar to that seen in CD28, CTLA-4, and CD19. See Table 2.--

Please replace the paragraph on page 15, lines 13-17, with the following rewritten paragraph:

--Alignment of human MDL-1 (SEQ ID NO: 12) and mouse MDL-1 long form (SEQ ID NO: 14). Of particular interest are a very short intracellular domain, corresponding to residues 1-2; with the transmembrane domain running from about 6 to 27 possessing a charged amino acid at about residue 16. Three putative N-linked glycosylation sites correspond to residues 51, 146, and 153 of the mouse long form; the latter of which are conserved in the human sequence. Note that the mouse long form, relative to the short form, appears to contain a spacer segment of about 25 amino acids.--

Please replace the paragraph beginning on page 16, line 1, with the following rewritten paragraph:

-- As used herein, the term "human DAP12" shall refer, when used in a protein context, to a protein having the primate amino acid sequence shown in Table 1 of SEQ ID NO: 2. The present invention also encompasses proteins comprising a substantial fragment thereof, e.g., mutants and polymorphic variants, along with a human derived polypeptide which exhibits the same biological function or interacts with human DAP12 specific binding components. These binding components typically bind to a human DAP12 with high affinity, e.g., at least about 100 nM, usually better than about 30 nM, preferably better than about 10 nM, and more preferably at better than about 3 nM. Homologous proteins are found in species other than humans, e.g., primates. While most of the description below is directed to DAP12, similar methods and features may be analogously applicable to the DAP10 and MDL-1 genes. Many limitations directed to DAP12 will correspond to terms in reference to DAP10 and MDL-1, though specific limitations relevant to one gene, e.g., a length limitation, will not necessarily intended to apply to the others. --

Please replace the paragraph beginning on page 18, line 28, with the following rewritten paragraph:

-- The isolated human DAP and MDL DNA can be readily modified by nucleotide substitutions, nucleotide deletions, nucleotide insertions, and inversions of nucleotide stretches. These modifications will result in novel DNA sequences which encode useful antigens, their derivatives, or proteins having similar or antagonist activity. These modified sequences can be used to produce mutant antigens or to enhance expression. Enhanced expression may involve gene amplification, increased transcription, increased translation, and other mechanisms. Such mutant DAP12 derivatives include predetermined or site-specific mutations of the respective protein or its fragments. "Mutant DAP12" encompasses a polypeptide otherwise sharing important features of the human DAP12 as set forth above, but having an amino acid sequence which differs from that of DAP12 as found in nature, whether by way of deletion, substitution, or

insertion. In particular, "site specific mutant DAP12" is defined as having homology with an antigen of ~~Table 1~~ SEQ ID NO: 2, and as sharing relevant biological activities with those antigens. Similar concepts apply to different DAP12 proteins, particularly those found in various other mammals. As stated before, it is emphasized that descriptions are generally meant to encompass additional DAP and MDL proteins, not limited solely to the primate embodiment specifically discussed.--

Please replace the paragraph beginning on page 22, line 27, through page 23, line 7, with the following rewritten paragraph:

-- A solubilized DAP or MDL antigen of this invention can be used as an immunogen for the production of antisera or antibodies specific for the antigen or many fragments thereof. The purified antigens can be used to screen monoclonal antibodies or antigen-binding fragments prepared by immunization with various forms of impure preparations containing the protein. In particular, the term "antibodies" also encompasses antigen binding fragments of natural antibodies. The purified DAP or MDL can also be used as a reagent to detect antibodies generated in response to the presence of elevated levels of DAP, MDL, or cell fragments containing the antigen, both of which may be diagnostic of an abnormal or specific physiological or disease condition. Additionally, DAP or MDL fragments may also serve as immunogens to produce the antibodies of the present invention, as described immediately below. For example, this invention contemplates antibodies raised against amino acid sequences of, or encoded by nucleotide sequences ~~shown in, e.g., Table 1,2, or 3,~~ of SEQ ID NOs: 1-14 or fragments thereof. In particular, this invention contemplates antibodies having binding affinity to or being raised against specific fragments which are predicted to lie outside of the lipid bilayer, either extracellular or intracellular domains. Additionally, various constructs may be produced from fusion of a membrane associating segment to the otherwise extracellular exposed portion of the molecule. Other antigenic complexes may be used, including complexes of the DAP or MDL with a receptor partner.--

Please replace the paragraph beginning on page 28, line 5, with the following rewritten paragraph:

-- This invention contemplates use of isolated DNA or fragments to encode, e.g., a biologically active corresponding DAP12 polypeptide. In addition, this invention covers isolated or recombinant DNA which encodes a biologically active protein or polypeptide which is capable of hybridizing under appropriate conditions with the DNA sequences described herein. Said biologically active protein or polypeptide can be an intact DAP12, or fragment, and have an amino acid sequence encoded by a nucleic acid ~~shown in Table 1 of~~ SEQ ID NO: 1 or 5. Further, this invention covers the use of isolated or recombinant DNA, or fragments thereof, which encodes a protein which is homologous to a DAP12 or which was isolated using cDNA encoding human DAP12 as a PCR or hybridization probe. The isolated DNA can have the respective regulatory sequences in the 5' and 3' flanks, e.g., promoters, enhancers, poly-A addition signals, and others. --

Please replace the paragraph beginning on page 31, line 36, with the following rewritten paragraph:

--Substantial identity in the nucleic acid sequence comparison context means either that the segments, or their complementary strands, when compared, are identical when optimally aligned, with appropriate nucleotide insertions or deletions, in at least about 50% of the nucleotides, generally at least about 56%, more generally at least about 59%, ordinarily at least about 62%, more ordinarily at least about 65%, often at least about 68%, more often at least about 71%, typically at least about 74%, more typically at least about 77%, usually at least about 80%, more usually at least about 85%, preferably at least about 90%, more preferably at least about 95 to 98% or more, and in particular embodiments, as high at about 99% or more of the nucleotides. Alternatively, substantial identity exists when the segments will hybridize under selective hybridization conditions, to a strand, or its complement, typically using a sequence ~~derived from Table 1 of~~ SEQ ID NO: 1 or 5. Typically, selective hybridization will occur when there is at least about 55% homology over a stretch of at least about 14 nucleotides, preferably at

least about 65%, more preferably at least about 75%, and most preferably at least about 90%. See, Kanehisa (1984) Nuc. Acids Res. 12:203-213. The length of homology comparison, as described, may be over longer stretches, and in certain embodiments will be over a stretch of at least about 17 nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about 40 nucleotides, preferably at least about 50 nucleotides, and more preferably at least about 75 to 100 or more nucleotides, e.g., 125, 150, 200, 250, 300, etc.--

Please replace the paragraph beginning on page 48, line 3, with the following rewritten paragraph:

-- Two primers are designed according to the provided sequences. To increase the chances of obtaining PCR products, human THP-1 cells, Thl T cells, monocytes activated with LPS, IFN-γ and IL-10, or NK cells are used. A product is purified, subcloned into pCR™ vector (Invitrogen, San Diego CA), and then sequenced. See ~~Tables 1,2, and 3~~SEQ ID NO: 1,2, 5, 6, 7, 8, 9, 10, 11,12, 13, and 14.--

Please replace the paragraph beginning on page 48, line 35, with the following rewritten paragraph:

--Tables ~~1,2, and 3 sequences~~ SEQ ID NO: 5, 9, and 13 allow design of a probe or primer which will allow isolation of mouse counterparts. With the primate and rodent sequences, other species counterparts can be identified using conserved sequences, either nucleic acid or epitopes.--

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nichol can be reached at (571) 272-0835.

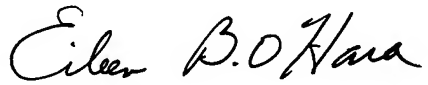
The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner



EILEEN B. O'HARA
PRIMARY EXAMINER